

The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows:

1. A drug delivery system, comprising:
 - a hydrogel formed from cyclodextrin and an amphiphilic copolymer, wherein the copolymer includes an A polymer block comprising a poly(alkylene oxide) and a B polymer block comprising a poly(hydroxyalkanoate); and
 - a therapeutically effective amount of at least one therapeutic agent intimately contained within the hydrogel.
2. The system of Claim 1, further comprising a pharmaceutically acceptable aqueous base.
3. The system of Claim 1, wherein the drug delivery system is injectable.
4. The system of Claim 3, wherein the hydrogel is thixotropic.
5. The system of Claim 1, wherein the system provides sustained release of the at least one therapeutic agent for a period of at least one week following initiation of drug release.
6. The system of Claim 1, wherein the system provides sustained release of the at least one therapeutic agent for a period of at least two weeks following initiation of drug release.
7. The system of Claim 1, wherein the poly(alkylene oxide) is selected from the group consisting of poly(ethylene oxide), poly(tetramethylene oxide) and poly(tetrahydrofuran).
8. The system of Claim 7, wherein the poly(alkylene oxide) is poly(ethylene oxide).
9. The system of Claim 1, wherein the poly(hydroxyalkanoate) is selected from the group consisting of: poly[(*R*)-3-hydroxybutyrate]; poly[(*R*)-4-hydroxybutyrate]; poly[(*R*)-3-hydroxyvalerate]; poly[(*R*)-3-hydroxybutyrate]-*co*-Poly[(*R*)-3-hydroxyvalerate]; poly[(*R*)-3-hydroxyhexanoate]; Poly[(*R*)-3-hydroxyheptanoate]; (*S*) enantiomers of each of such (*R*) enantiomers; racemic mixtures of such (*S*) and (*R*) enantiomers; and mixtures thereof.

10. The system of Claim 1, wherein the poly(hydroxyalkanoate) is selected from the group consisting of: poly[(*R*)-3-hydroxybutyrate]; poly[(*R*)-4-hydroxybutyrate]; (*S*) enantiomers of each of such (*R*) enantiomers; racemic mixtures of such (*S*) and (*R*) enantiomers; and mixtures thereof.

11. The system of Claim 1, wherein the poly(hydroxyalkanoate) comprises poly[(*R*)-3-hydroxybutyrate].

12. The system of Claim 1, wherein the copolymer is an amphiphilic triblock copolymer including a B polymer block mid-segment and two A polymer block end segments.

13. The system of Claim 12, wherein the poly(hydroxyalkanoate) B block polymer is selected from the group consisting of: poly[(*R*)-3-hydroxybutyrate]; poly[(*R*)-4-hydroxybutyrate]; poly[(*R*)-3-hydroxyvalerate]; poly[(*R*)-3-hydroxybutyrate]-*co*-Poly[(*R*)-3-hydroxyvalerate]; poly[(*R*)-3-hydroxyhexanoate]; Poly[(*R*)-3-hydroxyheptanoate]; (*S*) enantiomers of each of such (*R*) enantiomers; racemic mixtures of such (*S*) and (*R*) enantiomers; and mixtures thereof.

14. The system of Claim 12, wherein the poly(alkylene oxide) A block polymer is selected from the group consisting of poly(ethylene oxide), poly(tetramethylene oxide) and poly(tetrahydrofuran).

15. The system of Claim 14, wherein the poly(alkylene oxide) A block polymer is poly(ethylene oxide).

16. The system of Claim 15, wherein the poly(hydroxyalkanoate) B block polymer is selected from the group consisting of: poly[(*R*)-3-hydroxybutyrate]; poly[(*R*)-4-hydroxybutyrate]; poly[(*R*)-3-hydroxyvalerate]; poly[(*R*)-3-hydroxybutyrate]-*co*-Poly[(*R*)-3-hydroxyvalerate]; poly[(*R*)-3-hydroxyhexanoate]; Poly[(*R*)-3-hydroxyheptanoate]; (*S*) enantiomers of each of such (*R*) enantiomers; racemic mixtures of such (*S*) and (*R*) enantiomers; and mixtures thereof.

17. The system of Claim 1, wherein the poly(alkylene oxide) A block polymer and the poly(hydroxyalkanoate) B block polymer each has a molecular weight of from 500 to 20,000.

18. The system of Claim 1, wherein the poly(alkylene oxide) A block polymer and the poly(hydroxyalkanoate) B block polymer each has a molecular weight of from 2,000 to 10,000.

19. The system of Claim 1, wherein the poly(hydroxyalkanoate) B block polymer has a molecular weight of from 3,000 to 2,500.

20. The system of Claim 1, wherein the cyclodextrin is included at a level of from 5% to 80% of the weight of the copolymer.

21. The system of Claim 1, wherein the cyclodextrin is included at a level of from 5% to 50% of the weight of the copolymer.

22. The system of Claim 1, wherein the hydrogel comprises an aqueous solution containing the copolymer at a level of from about 1% to about 80% by weight.

23. The system of Claim 1, wherein the hydrogel comprises an aqueous solution containing the copolymer at a level of from about 10% to about 40% by weight.

24. The system of Claim 1, further comprising a secondary polymer which complexes with and/or conjugates the therapeutic agent.

25. The system of Claim 24, wherein the secondary polymer is a polymer selected from the group consisting of polyesters, polyurethanes, polyamides, polyethers, polysaccharides, poly(amino acid)s, polypeptides, and proteins.

26. The system of Claim 24, wherein the secondary polymer is a di- or mono-functional polymer with poly(ethylene glycol) segments.

27. The system of Claim 1, further comprising DNA nanospheres.

28. The system of Claim 1, wherein the copolymer has a molecular weight of between 1,000 and 50,000.

29. The system of Claim 1, wherein the copolymer has a molecular weight of between 5,000 and 35,000.

30. The system of Claim 1, wherein the at least one therapeutic agent is selected from the group consisting of peptides, proteins, small molecules, genes, antigens,

antibodies and fragments thereof and human recombinant proteins, DNA, RNA and DNA nanoparticles.

31. The system of Claim 1, wherein the at least one therapeutic agent is in a macromolecular form.

32. The system of Claim 1, wherein the at least one therapeutic agent is selected from the group consisting of analgesics, anesthetics, anti-arthritic drugs, disease modifying anti-rheumatic drugs, anti-asthma drugs, anticoagulants, anticonvulsants, antidepressants, antidiabetics, antineoplastics, antipsychotics, antihypertensives, antibiotics, antihistamines, decongestants, anti-inflammatories, muscle relaxants, anti-parasitic drugs, antiviral drugs, anti-restenotic agents, anti-spasm agents, chondroprotective agents, anti-adhesion agents, anti-tumor cell invasion agents, vasorelaxants, vasoconstrictors and immunosuppressants.

33. The system of Claim 1, wherein the at least one therapeutic agent is selected from the group consisting of peptides, proteins including cytokines, growth factors, angiogenesis factors, soluble receptors, antibodies and fragments thereof and human recombinant proteins, small molecules, genes, antigens including vaccines, DNA, RNA and DNA nanoparticles.

34. The system of Claim 1, wherein the hydrogel is applied to an implantable device.

35. The system of Claim 34, wherein the implantable device is selected from the group consisting of stents, catheters, airway tubes, conduits, screws, plates, shunts, artificial joints, artificial hearts, artificial valves and other prostheses.

36. A drug delivery system, comprising:
a hydrogel formed from cyclodextrin and an amphiphilic copolymer, wherein the copolymer includes an A polymer block comprising poly(ethylene oxide) and a B polymer block comprising poly(hydroxybutyrate); and
a therapeutically effective amount of at least one therapeutic agent intimately contained within the hydrogel.

37. The system of Claim 36, wherein the poly(hydroxybutyrate) comprises poly[(R)-3-hydroxybutyrate].

38. The system of Claim 36, wherein the at least one therapeutic agent is selected from the group consisting of peptides, proteins including cytokines, growth factors, angiogenesis factors, soluble receptors, antibodies and fragments thereof and human recombinant proteins, small molecules, genes, antigens including vaccines, DNA, RNA and DNA nanoparticles.

39. A hydrogel comprising cyclodextrin and an amphiphilic copolymer, wherein the copolymer includes an A polymer block comprising a poly(alkylene oxide) and a B polymer block comprising a poly(hydroxyalkanoate).

40. The hydrogel of Claim 39, further comprising an aqueous base.

41. The hydrogel of Claim 39, wherein the poly(alkylene oxide) is selected from the group consisting of poly(ethylene oxide), poly(tetramethylene oxide) and poly(tetrahydrofuran).

42. The hydrogel of Claim 41, wherein the poly(alkylene oxide) is poly(ethylene oxide).

43. The hydrogel of Claim 39, wherein the poly(hydroxyalkanoate) is selected from the group consisting of: poly[(*R*)-3-hydroxybutyrate]; poly[(*R*)-4-hydroxybutyrate]; poly[(*R*)-3-hydroxyvalerate]; poly[(*R*)-3-hydroxybutyrate]-*co*-Poly[(*R*)-3-hydroxyvalerate]; poly[(*R*)-3-hydroxyhexanoate]; Poly[(*R*)-3-hydroxyheptanoate]; (*S*) enantiomers of each of such (*R*) enantiomers; racemic mixtures of such (*S*) and (*R*) enantiomers; and mixtures thereof.

44. The hydrogel of Claim 39, wherein the poly(hydroxyalkanoate) is selected from the group consisting of: poly[(*R*)-3-hydroxybutyrate]; poly[(*R*)-4-hydroxybutyrate]; (*S*) enantiomers of each of such (*R*) enantiomers; racemic mixtures of such (*S*) and (*R*) enantiomers; and mixtures thereof.

45. The hydrogel of Claim 39, wherein the poly(hydroxyalkanoate) comprises poly[(*R*)-3-hydroxybutyrate].

46. The hydrogel of Claim 39, wherein the copolymer is an amphiphilic triblock copolymer including a B polymer block mid-segment and two A polymer block end segments.

47. A process for synthesizing an amphiphilic ABA triblock copolymer, including poly(ethylene oxide) as an A block polymer and poly(3-hydroxyalkanoate) as a B block polymer, the process comprising:

converting poly(3-hydroxyalkanoate) into telechelic poly(3-hydroxyalkanoate)-diol with a lower molecular weight;

producing methoxy-poly(ethylene oxide)-monocarboxylic acid from methoxy-poly(ethylene oxide); and

coupling the poly(3-hydroxyalkanoate)-diol with the methoxy-poly(ethylene oxide)-monocarboxylic acid using 1,3-dicyclohexylcarbodiimide to yield the ABA triblock copolymer.

48. The process of Claim 47, wherein the poly(3-hydroxyalkanoate) is poly(3-hydroxybutyrate) and the poly(3-hydroxyalkanoate)-diol is poly(3-hydroxybutyrate)-diol.

49. The process of Claim 47, wherein the poly(3-hydroxyalkanoate) is converted into telechelic poly(3-hydroxyalkanoate)-diol by a transesterification reaction with ethylene glycol.

50. The process of Claim 47, wherein the methoxy-poly(ethylene oxide)-monocarboxylic acid is produced by reacting methoxy-poly(ethylene oxide) with succinic anhydride in the presence of 4-(dimethylamino)pyridine and triethylamine in 1,4-dioxane.

51. The process of Claim 47, wherein the poly(3-hydroxyalkanoate)-diol and the methoxy-poly(ethylene oxide)-monocarboxylic acid are dried prior to coupling.

52. The process of Claim 47, wherein the poly(3-hydroxyalkanoate)-diol and the methoxy-poly(ethylene oxide)-monocarboxylic acid are coupled in dried methylene chloride.

53. The process of Claim 52, wherein the poly(3-hydroxyalkanoate)-diol and the methoxy-poly(ethylene oxide)-monocarboxylic acid are coupled in dried methylene chloride under a nitrogen atmosphere.

54. The process of Claim 47, wherein the poly(3-hydroxyalkanoate)-diol and the methoxy-poly(ethylene oxide)-monocarboxylic acid are coupled with an excess of the methoxy-poly(ethylene oxide)-monocarboxylic acid.

55. The process of Claim 47, further comprising isolating the ABA triblock copolymer using mixed solvents selected from the group consisting of methanol/diethyl ether and chloroform/diethyl ether.

56. The product produced by the process of Claim 47.

57. A process for forming a hydrogel drug delivery system, comprising combining cyclodextrin, a therapeutically effective amount of at least one therapeutic agent in an aqueous base fluid, and an amphiphilic copolymer, wherein the copolymer includes an A polymer block comprising a poly(alkylene oxide) and a B polymer block comprising a poly(hydroxyalkanoate).

58. The product produced by the process of Claim 57.

59. A method of treating a human or other mammal in need thereof with at least one therapeutic agent, comprising:

administering the at least one therapeutic agent in a drug delivery system, the drug delivery system comprising a hydrogel formed from cyclodextrin and an amphiphilic copolymer, wherein the copolymer includes an A polymer block comprising a poly(alkylene oxide) and a B polymer block comprising a poly(hydroxyalkanoate), wherein a therapeutically effective amount of the at least one therapeutic agent is intimately contained within the hydrogel.

60. The method of Claim 59, wherein the drug delivery system administered further comprises a pharmaceutically acceptable injectable aqueous base.

61. The method of claim 59, wherein the drug delivery system is administered intraarticularly, intravascularly, into the urogenital tract, subcutaneously, intramuscularly, intradermally, intracranially, intrapericardially, intrapleurally, or into any body cavity or potential space within the body.

62. The method of claim 61, wherein the drug delivery system is administered by injection.

63. The method of claim 59, wherein the drug delivery system is administered into a joint, a urogenital structure, a vascular structure, a pericardial space, a pleural space, a body cavity or a potential space within the body.

64. The method of claim 63, wherein the drug delivery system is administered by a catheter, syringe or implantable device.

65. The method of claim 59, wherein the drug delivery system is administered topically.

66. The method of Claim 59, wherein the at least one therapeutic agent is selected from the group consisting of peptides, proteins, small molecules, genes, antigens, antibodies and fragments thereof and human recombinant proteins, DNA, RNA and DNA nanoparticles.

67. The method of Claim 59, wherein the at least one therapeutic agent administered is in a macromolecular form.

68. The method of Claim 59, wherein the at least one therapeutic agent administered is selected from the group consisting of analgesics, anesthetics, anti-arthritic drugs, disease modifying anti-rheumatic drugs, anti-asthma drugs, anticoagulants, anticonvulsants, antidepressants, antidiabetics, antineoplastics, antipsychotics, antihypertensives, antibiotics, antihistamines, decongestants, anti-inflammatories, muscle relaxants, anti-parasitic drugs, antiviral drugs, anti-restenotic agents, anti-spasm agents, chondroprotective agents, anti-adhesion agents, anti-tumor cell invasion agents, vasorelaxants, vasoconstrictors and immunosuppressants.

69. The method of Claim 59, wherein the at least one therapeutic agent administered is selected from the group consisting of peptides, proteins, small molecules, genes, antigens, antibodies and fragments thereof and human recombinant proteins, DNA, RNA and DNA nanoparticles.

70. A drug delivery system, comprising:

micelles formed from an amphiphilic ABA copolymer, wherein the copolymer includes A polymer blocks comprising a poly(alkylene oxide) and a B polymer block comprising a poly(hydroxyalkanoate) selected from the group consisting of poly[(*R*)-3-hydroxybutyrate], poly[(*R*)-4-hydroxybutyrate], (*S*) enantiomers of each of such (*R*) enantiomers, racemic mixtures of such (*S*) and (*R*) enantiomers, and mixtures thereof; and
a therapeutically effective amount of at least one therapeutic agent intimately contained within the micelles.

71. The system of Claim 70, further comprising a pharmaceutically acceptable aqueous base.

72. The system of Claim 71, wherein the micelles are in sufficient concentration in the aqueous base to form a hydrogel.

73. The system of Claim 72, wherein the hydrogel is applied to an implantable device.

74. The system of Claim 73, wherein the implantable device is selected from the group consisting of stents, catheters, airway tubes, conduits, screws, plates, shunts, artificial joints, artificial hearts, artificial valves and other prostheses.

75. The system of Claim 70, wherein the system provides sustained release of the at least one therapeutic agent for a period of at least approximately one week following initiation of drug release.

76. The system of Claim 70, wherein the poly(alkylene oxide) is selected from the group consisting of poly(ethylene oxide), poly(tetramethylene oxide) and poly(tetrahydrofuran).

77. The system of Claim 76, wherein the poly(alkylene oxide) is poly(ethylene oxide).

78. The system of Claim 77, wherein the poly(hydroxyalkanoate) comprises poly[(R)-3-hydroxybutyrate].

79. The system of Claim 70, wherein the poly(hydroxyalkanoate) comprises poly[(R)-3-hydroxybutyrate].

80. The system of Claim 70, wherein the poly(alkylene oxide) A block polymer and the poly(hydroxyalkanoate) B block polymer each has a molecular weight of from 500 to 20,000.

81. The system of Claim 70, wherein the poly(alkylene oxide) A block polymer and the poly(hydroxyalkanoate) B block polymer each has a molecular weight of from 2,000 to 10,000.

82. The system of Claim 70, wherein the poly(hydroxyalkanoate) B block polymer has a molecular weight of from 3,000 to 2,500.

83. The system of Claim 70, further comprising a secondary polymer which complexes with and/or conjugates the therapeutic agent.

84. The system of Claim 70, wherein the micelles form nanoparticles or microparticles encapsulating the at least one therapeutic agent.

85. The system of Claim 70, wherein the copolymer has a molecular weight of between 1,000 and 50,000.

86. The system of Claim 70, wherein the copolymer has a molecular weight of between 5,000 and 35,000.

87. The system of Claim 70, wherein the at least one therapeutic agent is selected from the group consisting of peptides, proteins, small molecules, genes, antigens, antibodies and fragments thereof and human recombinant proteins, DNA, RNA and DNA nanoparticles.

88. The system of Claim 70, wherein the at least one therapeutic agent is in a macromolecular form.

89. The system of Claim 70, wherein the at least one therapeutic agent is selected from the group consisting of analgesics, anesthetics, anti-arthritis drugs, disease modifying anti-rheumatic drugs, anti-asthma drugs, anticoagulants, anticonvulsants, antidepressants, antidiabetics, antineoplastics, antipsychotics, antihypertensives, antibiotics, antihistamines, decongestants, anti-inflammatories, muscle relaxants, anti-parasitic drugs, antiviral drugs, anti-restenotic agents, anti-spasm agents, chondroprotective agents, anti-adhesion agents, anti-tumor cell invasion agents, vasorelaxants, vasoconstrictors and immunosuppressants.

90. The system of Claim 70, wherein the at least one therapeutic agent is selected from the group consisting of peptides, proteins including cytokines, growth factors, angiogenesis factors, soluble receptors, antibodies and fragments thereof and human recombinant proteins, small molecules, genes, antigens including vaccines, DNA, RNA and DNA nanoparticles.

91. The system of Claim 70, wherein the micelles are substantially stable within a temperature range of 15 degrees C to 45 degrees C.

92. A method of treating a human or other mammal in need thereof with at least one therapeutic agent, comprising:

administering the at least one therapeutic agent in a drug delivery system, the drug delivery system comprising micelles formed from an amphiphilic ABA copolymer, wherein the copolymer includes A polymer blocks comprising a poly(alkylene oxide) and a B polymer block comprising a poly(hydroxyalkanoate) selected from the group consisting of poly[(*R*)-3-hydroxybutyrate], poly[(*R*)-4-hydroxybutyrate], (*S*) enantiomers of each of such (*R*) enantiomers, racemic mixtures of such (*S*) and (*R*) enantiomers, and mixtures thereof, wherein a therapeutically effective amount of the at least one therapeutic agent is intimately contained within the micelles.

93. The method of Claim 92, wherein the drug delivery system administered further comprises a pharmaceutically acceptable injectable aqueous base.

94. The method of claim 92, wherein the drug delivery system is administered intraarticularly, intravascularly, into the urogenital tract, subcutaneously, intramuscularly, intradermally, intracranially, intrapericardially, intrapleurally, or into any body cavity or potential space of a body.

95. The method of claim 92, wherein the drug delivery system is administered by injection.

96. The method of claim 92, wherein the drug delivery system is administered into a joint, a urogenital structure, a vascular structure, a pericardial space, a pleural space, a body cavity or a potential space of a body.

97. The method of claim 96, wherein the drug delivery system is administered by a catheter, syringe or implantable device.

98. The method of claim 92, wherein the drug delivery system is administered topically.

99. The method of Claim 92, wherein the micelles form microparticles or nanoparticles that encapsulate the at least one therapeutic agent.

100. The method of Claim 92, wherein the at least one therapeutic agent is selected from the group consisting of peptides, proteins, small molecules, genes, antigens, antibodies and fragments thereof and human recombinant proteins, DNA, RNA and DNA nanoparticles.

101. The method of Claim 92, wherein the at least one therapeutic agent administered is in a macromolecular form.

102. The method of Claim 92, wherein the at least one therapeutic agent administered is selected from the group consisting of analgesics, anesthetics, anti-arthritic drugs, disease modifying anti-rheumatic drugs, anti-asthma drugs, anticoagulants, anticonvulsants, antidepressants, antidiabetics, antineoplastics, antipsychotics, antihypertensives, antibiotics, antihistamines, decongestants, anti-inflammatories, muscle relaxants, anti-parasitic drugs, antiviral drugs, anti-restenotic agents, anti-spasm agents, chondroprotective agents, anti-adhesion agents, anti-tumor cell invasion agents, vasorelaxants, vasoconstrictors and immunosuppressants.

103. The method of Claim 92, wherein the at least one therapeutic agent administered is selected from the group consisting of peptides, proteins, small molecules, genes, antigens, antibodies and fragments thereof and human recombinant proteins, DNA, RNA and DNA nanoparticles.